UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/155,982	10/09/98	KLEIN	F 032475-001

EXAMINER	
PORTNER, V	
ART UNIT	PAPER NUMBER
1645	10

DATE MAILED: 01/31/01

021839
BURNS DOANE SWECKER & MATHIS L L P
POST OFFICE BOX 1404
ALEXANDRIA VA 22313-1404

HM22/0131

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

1- File Copy

PTO-90C (Rev 2/95)

U.S. G.P.O. 1999 460-693

Jele

Office Action Summary

Application No.	Applicant(s)
09/155,982	Klein
Examiner	**Group Art Unit**
Portner	1645

☒ Responsive to communication(s) filed on *Nov 9, 2000*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *17-39* is/are pending in the application.

Of the above, claim(s) *20, 21, 23, 25, 27, 32, 36, 38, and 39* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *17-19, 22, 24, 26, 28-31, 33-35, and 37* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *17-39* are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claims 17-39 are pending.

Claims 20-21, 23,25,27,32,36,38-39 are drawn to a non-elected invention.

Claims 17-19,22,24,26,28-31,33-35 and 37 are under consideration.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

2. Applicant's election with traverse of Group I in Paper No. 6 was previously acknowledged. The traversal was submitted in paper number 9, based upon an asserted special technical feature that links all the claimed inventions, wherein this asserted special technical feature is defined to be T.equigenitalis specific monoclonal antibodies . This is not found persuasive because the claims are not so linked to form a single general inventive concept that defines a contribution considered over the prior art. Monoclonal antibodies to Taylorella were known in the prior art and made of record. The requirement is still deemed proper and was made FINAL in paper number 8.

Priority

3. The examiner appreciates the clarification provided by Applicant with respect to the numbering of claims, discussed at page 9, paragraph 2 of the Amendment. The Specification submitted and provided to the examiner set forth claims 1-16. The renumbering of the claims defined in the Office action, previously sent, was to assist in clear communication. The elected invention remains the same. Applicant is requested to make note of how the claims have been renumbered so any communication with respect to the claims can be clearly understood. See 37 CFR 1.126.

Rejections Withdrawn

4. Claims 18,19, 22,26-27,30,31, 35 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Objections/Rejections Maintained

5. Claim 24 rejected under 35 U.S.C. § 112, first paragraph as failing to provide an enabling disclosure.

6. Claims 17-19, 22, 24, 26-29, 31, 30,33-35 and 37 rejected under 35 U.S.C. 112, first paragraph, as containing subject

matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in **scope** with the instantly claimed invention.

7. The objection to the disclosure because of the noted informality at ~~page~~ page 24, line 11.

8.Claims 17,19, 22, 24, 26, 28 rejected under 35 U.S.C. 102(b) as being anticipated by Friedrich (1995).

9. Claims 17, 18, 19, 22, 24 rejected under 35 U.S.C. 102(b) as being anticipated by Akuzawa et al (1996).

10. Claim 18 rejected under 35 U.S.C. 103(a) as being unpatentable over Friedrich (1995) in view of Sugimoto et al (1988)

11. Claims 17, 19, 22, 24, 26, 28-29, 31, 35 and 37 rejected under 35 U.S.C. 103(a) as being unpatentable over Tainturier et al (1981) in view of Friedrich (1995) and Harlow:Antibodies, A Laboratory Manual (1988,chapters 4,6,9, 14-15).

12. Claims 30,33 and 34 rejected under 35 U.S.C. 103(a) as being unpatentable over Tainturier in view of Friedrich and Harlow further in view of Foster (US Pat. 4,444,879).

Response to Arguments

13. Applicant's arguments filed November 9, 2000 have been fully considered but they are not persuasive.

14. The rejection of claim 24 under 35 U.S.C. § 112, first paragraph as failing to provide an enabling disclosure is argued to be in error. It is asserted that the person skilled in the art would obtain a wide range of hybridomas of the invention and directs the examiner to the attached Deposit Declaration, Example 1, page 19 and page 6, lines 24-30 in support of the epitopes recited in the claims.

15. Upon consideration of the Deposit Declaration, the examiner noted that hybridoma identifier was set forth as 7C4. This number could not be found in the instant specification. The document for Yves Denouel, while signed, is not dated and therefore incomplete. Only a single hybridoma designated I-2536 was deposited. No monoclonal antibodies designated 7C4 or I-2536 were evaluated in Table II or III. What was deposited was not described in the instant specification.

It was also noted that Example 1 defines specific epitopes by specific monoclonal antibodies. These monoclonals produced by hybridomas have not been Deposited under the Budapest Treaty and therefore not publicly available. The Deposit requirement is maintained.

16. The rejection of claims 17-19, 22, 24, 26-29, 31, 30,33-36 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in **scope** with the instantly claimed invention is argued to be enabled through the description and teaching of the specification. The examiner is directed to Example 1, page 19 and page 6, lines 24-30.

17. Upon consideration of Example 1, page 19, lines 12-20, the examiner found that the epitopes of the invention were defined by multiple proteins and specific monoclonal antibodies that bind to the proteins.

The Illustrated Dictionary of Immunology,1995, page 102, defines the term: epitope as `an antigenic determinant. It is the simplest form or smallest structural area on a complex antigen molecule that can combine with an antibody or T-lymphocyte receptor.' Epitopes are not proteins, though proteins can contain many epitopes. The only definitions provided in the instant specification for the recited epitopes in the claims are defined by specific monoclonal antibodies. The bacterial species to which the monoclonal antibodies did not bind were 8 specific bacteria. These bacteria are not recited in the claims. The scope of the claims is not limited to the monoclonal antibodies used to describe the invention. Applicant's arguments are not commensurate in scope with the claimed invention.

Upon consideration of the disclosure at page 6, lines 24-30, the term: AcM was found. AcM was defined as that which allows the identification of a given epitope of the invention. The exact meaning of AcM was found at page 3, lines 33-36. This term refers to the monoclonal antibodies of the invention.

The epitopes are defined by the monoclonal antibodies and the monoclonal antibodies are defined by the epitopes. Circular reasoning does not structurally define specific epitopes. The epitopes of the instant specification have only been described by specific monoclonals. Deposit and limiting the claims to the deposited monoclonal antibodies would meet the definition of `AcM' set forth at page 6, lines 24-30 and page 3, lines 33-36. While monoclonal antibodies could be made and are enabled, the specific epitopes have only been described through specific binding of the monoclonal antibodies of the specification; the full scope of the claimed invention is not enabled.

18. The rejection of claims 17,19, 22, 24, 26, 28 under 35 U.S.C. 102(b) as being anticipated by Friedrich (1995) is argued by Applicant to not meet `the technical features of these monoclonal antibodies, and no indication regarding how to obtain them' nor is the specificity of Friedrich's monoclonal antibodies the specificity of Applicants monoclonal antibodies.

19. It is the position of the examiner that Friedrich teaches isolated monoclonal antibodies that were diagnostic of Taylorella equigenitalis infection. The antibodies were specific for diagnosis. The antibodies were monoclonal antibodies. The antibodies were obtained through using Taylorella equigenitalis as the immunizing antigen. The reference states that the monoclonal antibodies were diagnostic and gave better proof of infection caused by Taylorella equigenitalis. The immunogen of Friedrich is the same or equivalent immunogen as that used by Applicant. The antibodies of Fredrich, were specific diagnostic monoclonal antibodies. The specific monoclonals disclosed and argued are not claimed. Any monoclonal antibody specific to Taylorella equigenitalis is claimed.

By all comparable data, the monoclonal antibodies of the prior art inherently are the monoclonal antibodies of the claimed invention. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594. The prior art rejection is maintained for reasons of record.

20. The rejection of claims 17, 18, 19, 22, 24 under 35 U.S.C. 102(b) as being anticipated by Akuzawa et al (1996) is argued to "be a mere guess without legal basis." Applicant states "Moreover, applicants believe that an antigen of about 22-44 kDa would not be considered as corresponding to the 52.7 (LPS) kDa protein recited in claim 17."

21. Upon consideration of the arguments with respect to Akuzawa, it is the position of the examiner that Akuzawa et al does disclose monoclonal antibodies against outer membrane Taylorella equigenitalis epitopes. While, the examiner agrees with Applicant's argument that the 44 kDa antigen is not the now claimed 52.7 kDa protein, the reference still is applicable to the invention of monoclonal antibodies immunoreactive with a 22 kDa LPS antigen of Taylorella. The immunogen was Taylorella equigenitalis. This is not a guess. The English title states that the immunogen used to manufacture monoclonal antibodies to outermembrane antigens was Taylorella equigenitalis. The strain of Taylorella used was K-188 and the monoclonal antibodies (Mab) were designated NA-1 and NA-2. The reference does not leave the antigen relative molecular weight up to guess work. It clearly states in scientific nomenclature that 22-44 kDa was associated with T.equigenitalis Mab NA-1. LPS is recited in the abstract on

lines 5-6 from the bottom of the abstract. The monoclonal antibody was immunoreactive with LPS of about 28-44 kDa. The reference is a published document in a Japanese journal, 6 of the authors are associated with Nippon Vet. and Animal Science University (see abstract data, footnote number(1)).

By all comparable data, Akuzawa et al produced monoclonal antibodies immunoractive with Taylorella equigenitalis LPS of about 28-44 kDa. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594. The rejection made of record is maintained.

22. The rejection of claim 18 under 35 U.S.C. 103(a) as being unpatentable over Friedrich (1995)in view of Sugimoto et al (1988)is argued by asserting that Friedrich does not disclose monoclonal antibodies having the specificity claimed by Applicants and Sugimoto et al does not overcome or remedy Friedrich. Specific antigens of 52.7, 120 and 150(LPS)kDa are

argued. Figure 3 is asserted not to show the argued antigens of 52.7, 120 and 150(LPS)kDa.

23. It is the position of the examiner that, the claimed invention recites a number of antigens to which the genus of monoclonal antibodies may react. The claim limitations set forth antigens of relative molecular weights in kDa, and not exact molecular weights of each of the antigens. Relative molecular weights provide for about 10% variance in antigen weight determinations. A 50 kDa antigen could have a molecular weight of about from 45 kDa to about 54 kDa.

Friedrich clearly teaches the importance of producing monoclonal antibodies as diagnostic reagents. Sugimoto is cited for teaching major outer membrane antigens and the importance of immunological assays of these proteins to aid in diagnosis of infection. The presence of cross reactive antigens is discussed by Sugimoto and clearly suggests the development of effective, specific, sensitive serological tests for CEM. Friedrich teaches that monoclonal antibodies provide for `better proof' of infection.

The claimed invention is not limited to antigens of 120 and 150(LPS) kDa. Arguments directed to these specific antigens are not commensurate in scope with the claimed invention. Even if the claims were amended to recite just antigens of these two relative molecular weight molecules, Sugimoto teaches that

Taylorella equigenitalis produces immunostimulatory antigens from greater than 200 to about 29 kDa (see page 166, col. 1) which would include antigens of about 120 and 150 kDa.

Monoclonal antibodies could be obtained using methods known in the art, and the guidance, motivation and teaching provided by Friedrich and Sugimoto. The person of ordinary skill in the art would have been motivated to obtain and use monoclonal antibodies directed to the major outer membrane antigens of Taylorella equigenitalis(Sugimoto) for the purpose of better proof of diagnosis (Fredrich).

In decision Ex parte Erlich 3 USPQ2d 1011, case law was established for obviousness; specifically, it is obvious to make a monoclonal antibody to a known antigen for the purpose of attaining improved specificity of antibody binding.

24. The rejection of claim 18 under 35 U.S.C. 103(a) as being unpatentable over Friedrich (1995) in view of Corbel et al (1982) is argued by asserting that Friedrich does not disclose or suggest any T.equigenitalis specific antibodies, one antigen is assumed to be a polysaccharide and is about 180 kDa and that there is not scientific or legal basis to consider an 18 kDa H.equigenitalis polysaccharide as teaching a 22 (LPS)kDa antigen.

25. The asserted special technical feature of the claimed invention is monoclonal antibodies to Taylorella equigenitalis. Monoclonal antibodies to Taylorella equigenitalis antigens had been made prior to Applicant's invention by Friedrich. Corbel was sited by the examiner for teaching Taylorella equigenitalis antigens. While the examiner agrees that Corbel shows a 180 kDa LPS antigen which is not an 18 kDa antigen, the reference did not assume that the 180 kDa antigen is a lipopolysaccaride.

At page 534, Table 1, each of 11 immunoreactive antigens were analyzed for physical and chemical properties using art recognized methods of defining a protein, lipoprotein and lipopolysaccharide antigens. Corbel at the top of page 535, paragraph 1, states that lipid and glycoprotein antigens were identified. Antigens 1 and 2 were confirmed to be polysaccharide and lipopolysaccaride antigens, respectively. No guessing was involved. Clearly there is legal and scientific basis for the application of Corbel in an art rejection over the claimed invention directed to antibodies to Taylorella equigenitalis.

The antigen defined in column 2 of Table 1, is not an 18 kDa antigen, but an 180 kDa antigen which is a lipopolysaccaride. This reads on the about 150 kDa antigen of the claims. Corbel is very applicable to the claims that recite a 150 kDa antigen, as the nature of the antigen recited in the claims is not defined to

be a protein or lipopolysaccharide. Other antigens of about 25-50 kDa (see page 535, paragraph 5, last line) were described as being immunoreactive with antisera and also read on the claimed invention of 52.7 kDa. Arguments directed to a 22 kDa lipopolysaccaride of Corbel are convincing, but only in so far as the reference does not apply to this species of claimed antigen.

Corbel clearly is applicable to the claimed invention through the disclosure of purified antibodies and immunoreactive antigens obtained from the same or equivalent source as the antigens used by Applicant. Corbel shows proteins, basic proteins, glycoproteins, polysaccharide and lipopolysaccharide antigens of Taylorella equigenitalis of about 50 kDa and 150 kDa. Friedrich in view of Corbel obviate the now claimed invention.

In decision Ex parte Erlich 3 USPQ2d 1011, case law was established for obviousness; specifically, it is obvious to make a monoclonal antibody to a known antigen for the purpose of attaining improved specificity of antibody binding.

26. The rejection of claims 17, 19, 22, 24, 26, 28-29, 31, 35 and 37 under 35 U.S.C. 103(a) as being unpatentable over Tainturier et al (1981) in view of Friedrich (1995) and Harlow is argued to not disclose or suggest any monoclonal antibodies, there is no disclosure of an isolated product which would recognize an epitope of a bacterium of the T.equigenitalis

species and asserts that Tainturier is devoid of relevance to the claimed invention. Friedrich is asserted to not disclose or suggest the claimed invention. Harlow is argued to not be specific to the claimed invention.

27. It is the position of the examiner that Tainturier provides essential disclosure in the development of specific diagnostic methods and reagents for Taylorella equigenitalis. Tainturier used immunostimulatory antigens to develop a method which specifically identifies Taylorella equigenitalis in a biological sample.

As both polyclonal and monoclonal antibodies bind to epitopes of an antigen, it is clear to the examiner that Tainturier teaches the existence of diagnostic epitopes present in Taylorella equigenitalis antigens. All the antibodies of Tainturier were isolated products that immunoreacted with epitopes.

Arguments that the epitopes of the claimed genus of monoclonal antibodies would not be present in any other bacteria known in the art of microbiology is not convincing because the monoclonal antibodies of the instant invention were evaluated against Taylorella equigenitalis and 8 other bacteria. The number of known species, strains and serotypes of bacteria that have been identified by microbiologists is far greater than those

evaluated. The specific epitopes argued are only described through the specific monoclonal antibodies of the specification which are not recited in the claims; other physical, biochemical or structural characteristics of the epitopes argued have not been identified.

The rejection of the claims *was not* made under 35 U.S.C. 102, but under 35 U.S.C. 103. Tainturier teaches the presence of immunodiagnostic epitopes for T.equigenitalis, the existence of antigen and antibody reagents, and teaches the importance of accurate diagnostic methods for Contagious equine metrititis.

In view of existence of monoclonal antibodies to T.equigenitalis, (Friedrich) the knowledge of how to make and use monoclonal antibodies (Harlow), it would have been obvious to modify the method of Tainturier in view of the teaching and reagents of Friedrich and Harlow because Tainturier and Friedrich teach the importance of accurate diagnosis of Taylorella disease. The applied references obviate the claimed invention.

In decision Ex parte Erlich 3 USPQ2d 1011, case law was established for obviousness; specifically, it is obvious to make a monoclonal antibody to a known antigen for the purpose of attaining improved specificity of antibody binding.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on

combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant's arguments do not comply with 37 CFR 1.111 (C) because they do not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the references cited or the objections made. Further, they do not show how the amendments avoid such references or objections.

28. The rejection of claims 30, 33 and 34 under 35 U.S.C. 103(a) as being unpatentable over Tainturier in view of Friedrich and Harlow, further in view of Foster (US Pat. 4,444,879) is argued with respect to specific embodiments disclosed in Foster. Foster is asserted to not disclose monoclonal antibodies of the instant invention and is not asserted to overcome the deficiencies of Tainturier, Fredrich and Harlow.

29. As claims 30, 33 and 34 are directed to compositions of reagents, specifically kits, Foster et al was cited for what the reference taught with respect the formulation of kits, the packaging of immunological reagents into kit form.

The immunological reagents, and methods are described by Friedrich, Tainturier and Harlow, while Foster provided guidance and teaching for the formulation of kits. Foster, at column 15,

lines 12-34, teaches kits may comprise, an immunoassay container plate, immunoglobulin reagents, buffer solutions, powdered reagents to be solubilized, enzyme labels for Ig, substrate for the enzyme labels, positive and negative controls, pipettes for transfer of fluids, and a book of instructions for the immunoassay.

In view of Foster, it would have been obvious to incorporate immunoassay reagents into kit form. Ex parte Erlich, 3USPQ2d 1011, 1015 (CAFC 1987). The claimed invention is obviated for reasons of record in paper number 7.

30. Applicant stated that the pages previously sent were not clearly readable. Applicant's request for additional pages of Harlow is being provided and are attached hereto.

Conclusion

31. No claims are allowed.

32. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

33. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp
January 23, 2000

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600